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Original Article

Impact of birth weight on adult-onset diabetes mellitus in relation to current body mass index: The Japan Nurses' Health Study

Kota Katanoda [a,*], Mitsuhiko Noda [b,c], Atsushi Goto [d], Hideki Mizunuma [e], Jung Su Lee [f], Kunihiko Hayashi [g]

[a] Division of Cancer Statistics Integration, Center for Cancer Control and Information Services, National Cancer Center, Tokyo, Japan
[b] Department of Endocrinology and Diabetes, Saitama Medical University, Saitama, Japan
[c] Department of Diabetes Research, Diabetes Research Center, National Center for Global Health and Medicine, Tokyo, Japan
[d] Epidemiology and Prevention Group, Center for Public Health Sciences, National Cancer Center, Tokyo, Japan
[e] Fukushima Medical Center for Children and Women, Fukushima Medical University, Fukushima, Japan
[f] Department of Public Health, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan
[g] Department of Basic Allied Medicine, School of Health Science, Gunma University, Gunma, Japan

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ABSTRACT

Background: Although birth weight is considered as a fetal determinant of the development of adult-onset diabetes mellitus (DM), its public health importance relative to adult body mass index (BMI) remains unclear. We aimed to examine the association between adult-onset DM and birth weight in relation to adult BMI.
Methods: We conducted a self-administered questionnaire as a baseline survey of the Japanese Nurses' Health Study cohort between 2001 and 2007. Exclusion criteria were applied to the volunteer sample of 49,927 female nurses (age <30 years or unknown, current pregnancy, development of DM before the age of 30 years, unknown core variables), and data from 26,949 female nurses aged 30 years or older were used. The association between history of DM diagnosis and birth weight was analyzed using logistic regression.
Results: A linear inverse association was observed between birth weight and DM, after adjustment for age, BMI, and parental history of DM. The odds ratio for developing DM per 100 g increase in birth weight was 0.93 (95% confidence interval [CI], 0.90–0.96). The association was unchanged when birth weight was converted to percentile for gestational age. In the BMI-stratified analysis, the odds ratio for DM in the <2500 g birth weight group reached 4.75 (95% CI, 1.22–18.44, compared to the reference 3000–3499 g group) among women with normal low BMI (18.5–20.9).
Conclusions: Birth weight and its percentile for gestational age were associated with adult-onset DM. Attention should be paid to the risk of DM among women born with low weight, even when their current BMI is normal.

Introduction

Adult-onset diabetes mellitus (DM) is a major global medical burden. Globally, an estimated 1.3 million deaths were attributed to DM in 2010, twice as many as in 1990.[1] There have been systematic reviews of the association between birth weight and adult-onset DM,[2,3] one of which reported that the risk of DM decreased by 30% for every 1 kg increase in birth weight.[3] Although the finding provided support for the theory of fetal origins of adult disease,[4] the impact of birth weight in relation to adult body mass index (BMI) is still unknown. Obesity in adulthood is a major risk factor for DM. The effect of birth weight on adult-onset DM is reported to vary depending on BMI in adulthood.[5] According to the above-mentioned systematic review, the association between birth weight and DM is weaker in people with a higher current BMI.[3]

* Corresponding author. Center for Cancer Registries, Center for Cancer Control and Information Services, National Cancer Center, 5-1-1 Tsukiji, Chuo-ku, Tokyo, 104-0045, Japan.
E-mail address: kkatanod@ncc.go.jp (K. Katanoda).
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However, important questions have not been addressed, such as whether we should be cautious about developing DM even when current BMI is normal, and how DM risk changes according to the combination of birth weight and current BMI levels.[5]

The association between birth weight and adult-onset DM is biologically explained as an adaptation to intrauterine undernutrition.[4] If this hypothesis is true, the effect of being small for gestational age will be more important. Although the association between birth weight and DM has been reported in many studies, few studies have investigated the effect of fetal growth on the development of DM.[6]

In Japan, the prevalence of low birth weight has been increasing. According to the national statistics from 2012, the proportions of infants with a birth weight of less than 2500 g were 8.5% in males and 10.7% in females. These proportions were almost double those from 1980 (4.8% in males and 5.6% in females).[7] Estimation of the impact of birth weight on later life is needed to evaluate the public health burden of the increasing prevalence of low birth weight.

The present study aimed to examine the association between adult-onset DM and birth weight using data from a cohort of Japanese female nurses. To clarify the meaning of the association in the practice of public health and obstetrics, current BMI categories were used as adjustment, stratification, or combined independent variables, and the effect of birth weight for gestational age was examined using percentile score based on fetal growth curve.

Materials and methods

Data

The baseline data from the cohort of the Japanese Nurses' Health Study (JNHS) were used. JNHS is an ongoing prospective cohort study in female nurses that was started in 2001.[8] The baseline survey, which used a self-administered questionnaire, was conducted from 2001 to 2007, and responses were obtained from 49,927 female nurses. The participants of the present study were female nurses aged 30 years or older. After the following exclusion criteria were applied, the analytic cohort included 26,949 women: age <30 years or unknown (2179 women), current pregnancy (944 women), unknown DM status (53 women), development of DM before the age of 30 years (37 women), unknown birth weight (19,328 women), and unknown current BMI (437 women).

Variables

The variables used in the present study were history of adult-onset DM diagnosis, birth weight (four categories: <2500 g, 2500–2999 g, 3000–3499 g, and ≥3500 g), current BMI (six categories: <18.5, 18.5–20.9, 21.0–22.9, 23.0–24.9, 25.0–26.9, and ≥27.0 kg/m^2), and maternal or paternal history of DM.

History of a DM diagnosis was determined via the question "Have you ever been diagnosed with diabetes by a physician?" For this question, gestational diabetes was explicitly excluded. As stated above, we excluded participants diagnosed with diabetes before age 30 and classified the remaining cases as adult-onset DM cases.

Percentiles of birth weight for gestational age were calculated based on the Japanese neonatal anthropometric charts.[9] Specifically, from the birth weight and gestational age at birth of each participant, a z-score of birth weight was determined using the LMS method proposed by Cole.[10] The z-scores were converted into percentile scores on the assumption of a normal distribution. Percentile scores were used because they are widely used in obstetric practice to evaluate intrauterine nutritional status. Smoking status (three categories: current smoker, former smoker, and nonsmoker) was also used in stratified analysis. Women with unknown gestational age (8701 women) and those with an extremely high percentile score (>99.9%) or an extremely low percentile score (<0.1%) (703 women) were excluded from the statistical analyses that included the percentile score. We applied this exclusion criterion because several unrealistic combinations of gestational age and birth weight were found in both extreme ends. We confirmed in a preliminary analysis including all data that this exclusion did not affect our main result.

Statistical analysis

Logistic regression analysis was performed with adult-onset DM status as the dependent variable and birth weight as the independent variable. An age-adjusted model, an age- and current BMI-adjusted model (model 1), and a model additionally adjusted for maternal/paternal history of DM (model 2) were applied. Stratified analyses were performed according to BMI, presence or absence of maternal/paternal history of DM, and smoking status. The 3000–3499 g birth weight category was used as the reference. Because there were few women in the BMI category of <18.5 kg/m^2 and the category of former smokers, these categories were excluded from the stratified analyses on the association between birth weight and adult-onset DM. For the analysis of birth weight percentile, BMI categories with small numbers of participants were rounded (18.5–21.9 and 22.0–24.9 kg/m^2 for stratified analysis according to BMI; <21.0 kg/m^2 for other stratified analysis). To examine the effect of large birth weight in detail, an additional analysis was done in which the highest birth weight group was divided into two categories (3500–3999 g and ≥4000 g).

In order to compare the effects between birth weight and BMI, a model using a combination of birth weight and current BMI as the independent variable was applied. The participants were classified into a total of 16 categories according to the combination of the four birth weight categories and the four BMI categories (18.5–20.9, 21.0–22.9, 23.0–24.9, and ≥25.0 kg/m^2). The combined category of BMI of 18.5–20.9 kg/m^2 and birth weight of 3000–3499 g was used as a reference to calculate odds ratios because the category was most frequent within the normal or ordinary range.

Logistic regression analysis was also performed with birth weight percentile as the independent variable and adult-onset DM status as the dependent variable. Birth weight percentiles were divided into five categories: <10th, 10th–29th, 30th–69th (reference), 70th–89th, and ≥90th.

In order to check the validity of the outcome variable, sensitivity analysis was performed using a dependent variable of DM defined by a combination of data, including a fasting plasma glucose level of ≥126 mg/dL and the use of DM drugs, obtained from the baseline questionnaire survey. Analysis including only women with DM diagnosed within the previous 3 years was also done.

Ethical approval for the study was obtained from the Ethics Review Committees of the Faculty of Medicine, Gunma University and the National Institute of Public Health.

Results

Table 1 shows the characteristics of the participants according to the birth weight categories. The number of women was largest in the 3000–3499 g birth weight group (43.0%) and smallest in the <2500 g group (8.8%). Mean age decreased as birth weight increased (linear trend, $p < 0.001$). The mean gestational age increased as birth weight increased (linear trend, $p < 0.001$). There was a U-shaped association between current BMI and birth weight (quadratic trend, $p < 0.001$), and the 2500–2999 g birth weight group had the lowest current BMI. Current smokers accounted for